

25

study, a formulation of the invention in capsules comprising 50 mg of progesterone and 2 mg estradiol was used. The two formulations comprised:

The dissolution study was performed using a USP dissolution apparatus (reciprocating cylinder) ("USP Apparatus 3"). The apparatus was set to 30 dips per minute. 250 mL of a solution of 0.1N HCl with 3% sodium lauryl sulfate was used at 37 C.

In both studies, progesterone was dissolved faster, and with smaller standard deviations, from the capsules of the invention than from Prometrium. Dissolution of estradiol was comparable but marginally slower from the capsules of the invention than from Estrace. For illustrative purposes, a graph showing progesterone dissolution from the 200 mg progesterone capsule of the invention and from Prometrium is attached as FIG. 5.

Both capsules of the invention were stable on storage in white HDPE bottles. Positive stability data were obtained with the 200 mg progesterone formulation over 6 months (>6 months data unavailable) and with the 50 mg progesterone formulation over 3 months (>3 months data unavailable).

It will be apparent to those skilled in the art that various modifications and variations can be made in the present disclosure without departing from the spirit or scope of the disclosure. Thus, it is intended that the present disclosure cover the modifications and variations of this disclosure provided they come within the scope of the appended claims and their equivalents.

Likewise, numerous characteristics and advantages have been set forth in the preceding description, including various alternatives together with details of the structure and function of the devices and/or methods. This disclosure is intended as illustrative only and as such is not intended to be exhaustive. It will be evident to those skilled in the art that various modifications may be made, especially in matters of structure, materials, elements, components, shape, size and arrangement of parts including combinations within the principles of the disclosure, to the full extent indicated by the broad general meaning of the terms in which the appended claims are expressed. To the extent that these various modifications do not depart from the spirit and scope of the appended claims, they are intended to be encompassed therein.

We claim:

1. A pharmaceutical composition comprising:
a solubilizing agent, the solubilizing agent comprising an effective amount of a C6-C12 oil;
1.0 mg estradiol or 1.03 mg estradiol hemihydrate, the estradiol or estradiol hemihydrate being at least about 90% solubilized in the solubilizing agent; and
100 mg progesterone;
wherein the estradiol or the estradiol hemihydrate, and the progesterone are uniformly dispersed in the solubilizing agent.
2. The pharmaceutical composition of claim 1, wherein the solubilizing agent is selected from at least one of monoglycerides, diglycerides, triglycerides, and combinations thereof, wherein the monoglycerides, diglycerides, and triglycerides are predominantly of C6-C12 fatty acid chain lengths.
3. The pharmaceutical composition of claim 2, wherein the monoglycerides, diglycerides, and triglycerides are >50% C6-C12 fatty acid chain lengths.

26

4. A pharmaceutical composition comprising:

about 100 mg progesterone;
about 1.0 mg estradiol or 1.03 mg estradiol hemihydrate, the estradiol or estradiol hemihydrate being at least about 90% solubilized;
about 195.97 mg of monoglycerides and diglycerides of caprylic acid and capric acid (CAPMUL MCM); and
about 3.0 mg of at least one of lauroyl macrogol-32 glycerides EP, lauroyl polyoxyl-32 glycerides NF, or lauroyl polyoxylglycerides (GELUCIRE 44/14);
wherein the estradiol or the estradiol hemihydrate, and the progesterone are uniformly dispersed in the solubilizing agent.

5. A method of treating a menopause-related symptom in a woman comprising administering an effective amount of pharmaceutical composition to a subject in need thereof, the pharmaceutical composition comprising:

about 100 mg progesterone;
about 1.0 mg estradiol or 1.03 mg estradiol hemihydrate, the estradiol or estradiol hemihydrate being at least about 90% solubilized;
about 195.97 mg of monoglycerides and diglycerides of caprylic acid and capric acid (CAPMUL MCM); and
about 3.0 mg of at least one of lauroyl macrogol-32 glycerides EP, lauroyl polyoxyl-32 glycerides NF, or lauroyl polyoxylglycerides (GELUCIRE 44/14);
wherein the estradiol or the estradiol hemihydrate, and the progesterone are uniformly dispersed in the solubilizing agent.

6. The method of claim 5, wherein the pharmaceutical composition is administered as a continuous-combined therapy regimen.

7. The method of claim 5, wherein the pharmaceutical composition is administered a sequentially-combined therapy regimen.

8. A method of treating a vasomotor symptom in a woman comprising administering an effective amount of a pharmaceutical composition comprising:

1.0 mg estradiol or 1.03 mg estradiol hemihydrate, the estradiol or estradiol hemihydrate being at least about 90% solubilized in the solubilizing agent;
100 mg progesterone; and
a solubilizing agent, the solubilizing agent comprising an effective amount of a C6-C12 oil;
wherein the estradiol or the estradiol hemihydrate, and the progesterone are uniformly dispersed in the solubilizing agent; and

wherein the pharmaceutical composition is administered once daily for the treatment of symptoms associated with menopause.

9. The method of claim 8, wherein the pharmaceutical composition is administered as a continuous-combined therapy regimen.

10. The method of claim 8, wherein the pharmaceutical composition is administered as a sequentially-combined therapy regimen.

11. The method of claim 8, wherein the solubilizing agent is selected from at least one of monoglycerides, diglycerides, triglycerides, and combinations thereof, wherein the monoglycerides, diglycerides, and triglycerides are predominantly of C6-C12 fatty acid chain lengths.

12. The method of claim 11, wherein the monoglycerides, diglycerides, and triglycerides are >50% C6-C12 fatty acid chain lengths.

* * * * *